DEPARTMENT OF THE AIR FORCE
59TH MEDICAL WING (AETC)
JOINT BASE SAN ANTONIO - LACKLAND TEXAS

30 NOV 2016

MEMORANDUM FOR GE
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FROM: 59 MDW/SGVU

SUBJECT: Professional Presentation Approval

1. Your journal, entitled **Clinical indicators associated with HIV acquisition in the United States Air Force** published in **Aids Care** in accordance with MDWI 41-108, has been approved and assigned local file #**16403.**

2. Pertinent biographic information (name of author(s), title, etc.) has been entered into our computer file. Please advise us (by phone or mail) that your presentation was given. At that time, we will need the date (month, day and year) along with the location of your presentation. It is important to update this information so that we can provide quality support for you, your department, and the Medical Center commander. This information is used to document the scholarly activities of our professional staff and students, which is an essential component of Wilford Hall Ambulatory Surgical Center (WHASC) internship and residency programs.

3. Please know that if you are a Graduate Health Sciences Education student and your department has told you they cannot fund your publication, the 59th Clinical Research Division may pay for your basic journal publishing charges (to include costs for tables and black and white photos). We cannot pay for reprints. If you are 59 MDW staff member, we can forward your request for funds to the designated wing POC.

4. Congratulations, and thank you for your efforts and time. Your contributions are vital to the medical mission. We look forward to assisting you in your future publication/presentation efforts.

Linda Steel-Goodwin

LINDA STEEL-GOODWIN, Col, USAF, BSC
Director, Clinical Investigations & Research Support

PROCESSING OF PROFESSIONAL MEDICAL RESEARCH/TECHNICAL PUBLICATIONS/PRESENTATIONS

1. TO: CLINICAL RESEARCH	2. FROM: (Author's Name, Rank, Grade, Office Symbol)	3. GME/GHSE STUDENT:	4. PROTOCOL NUMBER:
	William N Hannah Jr, Col, USAF, MC, 59 MDW/GE	☐ YES ☒ NO	WRAIR #1898

5. PROTOCOL TITLE: (**NOTE:** For each new release of medical research or technical information as a publication/presentation, a new 59 MDW Form 3039 must be submitted for review and approval.)

Epidemiology and Risk Factors for HIV Infection in U.S. Air Force Service Members, 1996-2011

6. TITLE OF MATERIAL TO BE PUBLISHED OR PRESENTED:

Clinical indicators associated with HIV acquisition in the United States Air Force

7. FUNDING RECEIVED FOR THIS STUDY? ☒ YES ☐ NO FUNDING SOURCE: Henry Jackson Foundation (W81XWH-11-2-0174)

8. DO YOU NEED FUNDING SUPPORT FOR PUBLICATION PURPOSES: ☐ YES ☒ NO

9. IS THIS MATERIAL CLASSIFIED? ☐ YES ☒ NO

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AIDS CARE

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17. IS A 502 ISG/JAC ETHICS REVIEW REQUIRED (JER DOD 5500.07-R)? ☐ YES ☒ NO

I CERTIFY ANY HUMAN OR ANIMAL RESEARCH RELATED STUDIES WERE APPROVED AND PERFORMED IN STRICT ACCORDANCE WITH 32 CFR 219, AFMAN 40-401_IP, AND 59 MDWI 41-108. I HAVE READ THE FINAL VERSION OF THE ATTACHED MATERIAL AND CERTIFY THAT IT IS AN ACCURATE MANUSCRIPT FOR PUBLICATION AND/OR PRESENTATION.

18. AUTHOR'S PRINTED NAME, RANK, GRADE	19. AUTHOR'S SIGNATURE	20. DATE
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PROCESSING OF PROFESSIONAL MEDICAL RESEARCH/TECHNICAL PUBLICATIONS/PRESENTATIONS

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29. COMMENTS ☒ APPROVED ☐ DISAPPROVED

IRB approved exempt study with appropriate disclaimers. Approved

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Clinical indicators associated with HIV acquisition in the United States Air Force

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Abstract:

Mandatory HIV screening of United States Air Force (USAF) personnel every 2 years effectively identifies incident cases, however testing frequency limits the ability to detect early HIV infection. Identifying clinical indicators of HIV in the USAF population is necessary to develop a supplemental provider-based targeted testing strategy. We conducted a matched case-control study of male active duty USAF personnel with a new HIV diagnosis (n=452) between 1996 and 2011 matched to five randomly selected controls (n=2,176). The relationship between clinical diagnoses, determined by ICD-9 codes, and HIV infection was assessed using conditional logistic regression. In unadjusted analyses of ICD-9 codes ever and within the last 2 years before HIV diagnosis, the conditional odds of HIV infection were greater in those with clinical signs and symptoms of HIV (cOR 5.05, 95% CI 4.00-6.39), mental health diagnoses (cOR 2.61, 95% CI 1.86-3.67), and STI diagnoses (cOR 2.33, 95% CI 1.50-3.60). Compared to those with ≤10 medical encounters in the 2 years prior to HIV diagnosis, individuals with 11-35 medical encounters (cOR 2.19, 95% CI 1.73-2.79) and >35 medical encounters (cOR 4.15, 95% CI 2.69-6.39) had a higher odds of HIV acquisition. In multivariate analyses, clinical signs and symptoms of HIV within the last 2 years of HIV diagnosis (cOR 4.10, 95% CI 3.22-5.22) and ever having a mental health diagnosis (cOR 1.97, 95% CI 1.44-2.70) remained significant ($p<0.01$). Clinical encounters, particularly those featuring clinical signs and symptoms of HIV or a history of mental health complaints, provide an opportunity for targeted testing as a supplement to mandated testing at 2-year intervals. Provider education to increase HIV testing in persons at risk would enhance early HIV diagnosis and potentially reduce forward transmission in the USAF population.

Key Words: HIV, risk factors, mental health, targeted testing, and USAF

Introduction

The development of a successful human immunodeficiency virus type 1 (HIV-1) prevention program is dependent upon the identification of HIV risk factors in a population and the subsequent testing of at-risk individuals in order to provide effective education to reduce HIV acquisition and transmission. To detect incident cases of HIV, the United States Air Force (USAF) utilizes a system-wide approach with mandated HIV testing for all active duty members approximately every 2 years. Although mandated testing has the benefit of capturing nearly all cases of HIV infection, the testing frequency limits the ability to detect cases early in the course of infection compared with a targeted testing strategy.

Early detection of incident cases is important as individuals who are unaware of HIV infection account for approximately one-third of HIV transmissions in the U.S. (Skarbinski et al., 2015). This can be challenging since several HIV risk factors identified in the general population, including intravenous drug use (IDU) and illicit substance abuse, are mitigated in the US military due to accession standards and mandatory drug testing. Additionally, risk factor identification may be limited by members' concerns of self-disclosure, stigma of HIV diagnosis, military career impact, and possible disciplinary actions after the repeal of the "Don't Ask Don't Tell" policy (Katz, 2010).

There is the potential to identify HIV infection earlier and disrupt forward HIV transmission in approximately 75% of incident cases in the USAF since the majority of cases are identified as a result of mandated screening (Kugblenu, Paulin, Tastad, & Okulicz, 2016). A supplemental targeted testing strategy initiated by providers in clinical settings may be an effective method to improve early HIV diagnosis. It is important to inform providers by ascertaining clinical indicators of HIV infection in the USAF, as well as clinical diagnoses more

common in those with versus without HIV infection. We aim to characterize the clinical indicators associated with HIV infection in order to enhance supplemental provider-directed HIV screening in our population.

Methods

The USAF, in keeping with Department of Defense (DoD) policy, conducts compulsory HIV testing among applicants to USAF service and periodic (every 2 years) and peri-deployment testing among its personnel. In this nested case-control study, the study population consisted of all USAF personnel on active service at any time during the study period, January 1, 1996 through December 31, 2011 who had demographic data available. Among those eligible, all persons with a new HIV diagnosis during the study period were considered cases. Five randomly-selected controls were matched to each case by exact age, length of service (±3 months), sex, race, branch of the military, service component (active duty, National Guard, or Reservists), and HIV test collection date or index date. HIV testing data were obtained from the USAF School of Aerospace Medicine HIV Testing Service and demographic and clinical data were obtained from the Armed Forces Health Surveillance Center (AFHSC). This study was approved by the Walter Reed Army Institute of Research Institutional Review Board.

The relationship between clinical indicators and HIV infection was assessed in univariate analyses using conditional logistic regression. Cases missing a factor were excluded from analysis as were all matched controls and sensitivity analyses did not reveal significant differences in excluded subjects (data not shown). Data for clinical diagnoses were examined by International Classification of Disease, Ninth Revision (ICD-9) diagnostic codes and included sexually transmitted infection (STI) diagnosis, substance abuse, clinical signs and symptoms of HIV infection, clinical HIV syndrome, mental health disorder, psychosocial stressor, headache, sleep disorder, and co-occurring clinical syndromes ever and during the two years before the index date as previously described (Hakre et al., 2011). A final multivariate model for clinical factors was determined using forward and backward iterative stepwise selection of baseline

characteristics and clinical factors occurring prior to HIV diagnosis; a criteria p-value of 0.10 and 0.01 were used to enter and retain factors in the model, respectively. All analyses were performed using SAS version 9.3 (Cary, North Carolina).

Results

A total of 462 incident HIV cases were identified among USAF personnel who served on active duty between January 1, 1996 and December 31, 2011. Due to small numbers, the 10 female cases were removed and all descriptions and analyses are restricted to males (Table 1). In unadjusted analyses within the last 2 years before HIV diagnosis, having clinical signs and symptoms of HIV infection (conditional odds ratio [cOR] 5.05, 95% CI 4.00-6.39), having a clinical syndrome consistent with HIV (cOR 3.02, 95% CI 2.42-3.78), clinical history of a mental health disorder (cOR 2.61, 95% CI 1.86-3.67), or history of a STI (cOR 2.33, 95% CI 1.50-3.60) had significantly higher odds of HIV infection (Table 2). Compared to those with 10 or less medical encounters in the 2 years prior to HIV diagnosis, individuals with 11-35 medical encounters (cOR 2.19, 95% CI 1.73-2.79) and >35 medical encounters (cOR 4.15, 95% CI 2.69-6.39) had a higher odds of HIV acquisition. The most common ICD-9 codes for mental health issue, substance abuse, and STI prior to HIV diagnosis are shown for cases and controls (Figure 1).

In multivariate analyses, active duty personnel with a clinical syndrome of HIV (cOR 2.23, 95% CI 1.75-2.84) and having clinical signs and symptoms of HIV infection in the prior 2 years (cOR 4.10, 95% CI 3.22-5.22) had higher odds of HIV infection after adjusting for the factors above (Table 3). In addition, ever having a mental health diagnosis (cOR 1.97, 95% CI 1.44-2.70) also remained significant in multivariate analyses.

Discussion

The goal of this study was to identify and assess clinical indicators associated with HIV infection in the USAF. In multivariate analyses in the 2 years prior to HIV diagnosis, five indicators had significantly higher odds of HIV infection: having clinical signs and symptoms of HIV infection, a clinical syndrome consistent with HIV, more frequent medical encounters, clinical history of a mental health disorder and history of a STI. Given that delays in HIV diagnosis are common and opportunities for screening are missed, USAF providers should consider additional targeted HIV screening for patients with these clinical indicators in addition to mandated screening at 2-year intervals.

Numerous studies have demonstrated the clinical association between HIV infection and serious mental health illness, and the prevalence rate of HIV infection in patients with serious mental illness is higher than expected in the general population for the same demographic area (Collins, Holman, Freeman, & Patel, 2006; Kaltenthaler, Pandor, & Wong, 2014; Rosenberg et al., 2001; Wright, Akhtar, Tosh, & Clifton, 2014). Individuals with severe mental illness in the military, however, undergo an extensive evaluation process which ultimately results in separation from active duty for individuals deemed unfit for continued military service. The results of this study suggest that less debilitating forms of mental illness, such as depression, adjustment reactions, and anxiety may also play a contributory role in HIV acquisition in the active duty population. Mental illness has been linked to higher risk sexual activity such as alcohol and drug use, multiple sex partners, engaging in high-risk same-sex sexual activity, lack of condom use, trading sex for drugs or money, and engaging in sex while using psychoactive medications (Kaltenthaler et al., 2014; Meade & Sikkema, 2005; Rosenberg et al., 2001). This

study suggests that providers evaluating individuals with mental health complaints should consider a discussion of HIV risk behaviors and initiate testing if indicated.

In multivariate analyses, clinical syndrome of HIV in the previous 2 years, and having clinical signs and symptoms of HIV infection in the prior 2 years had higher conditional odds of HIV infection after adjusting for other clinical factors. Several studies have been published on missed opportunities in HIV screening in a variety of clinical settings. For example, one study noted that 47% of patients with newly diagnosed HIV infection had had at least 2 prior clinical encounters, with most experiencing HIV-related symptoms in at least one of those visits (Chin, Hicks, Samsa, & McKellar, 2013). A study in South Carolina found that the majority of persons with newly diagnosed HIV had multiple prior health care visits with only 21% likely to prompt a HIV test (Duffus et al., 2009). Thus, in the USAF population, these frequent medical encounters likely represent missed opportunities for HIV testing and education to mitigate possible HIV behavioral risk factors.

Limitations of this study include exclusive use of ICD-9 diagnosis codes as electronic health records were not available for the entire study period. Additionally, many of the clinical diagnoses associated with HIV seroconversion lack specificity and therefore have limited ability to provide explicit screening guidance. Databases do not include sexual risk behavior data which would also inform provider-based supplemental HIV screening in addition to the clinical indicators identified in this study. In conclusion, this study provides important information for USAF providers regarding clinical diagnoses associated with HIV acquisition in the USAF population. Provider education and training initiatives are currently underway to increase HIV testing in persons at risk to enhance early HIV diagnosis and potentially reduce forward transmission in the USAF population.

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Table 1. Demographic Characteristics

	Case	Control	Total
Number, n	452	2176	2628
Age at index, median (IQR)*	27 (23-34)	27 (23-33)	27(23-33)
Race*			
Black	210 (46.5%)	1,025 (47.1%)	1,235 (47.0%)
Other	35 (7.7%)	155 (7.1%)	190 (7.2%)
White	207 (45.8%)	996 (45.8%)	1,203 (45.8%)
Deployment within 2 years			
≥ 1 deployment	85 (18.8%)	654(30.1%)	739 (28.1%)
None	367 (81.2%)	1,522 (69.9%)	1,889(71.9%)
Military service time at index, years, median (IQR)	6.5 (3.0-12.0)	6.0 (2.9-11.5)	6.1 (2.9–11.6)
Marital status at index			
Married	92 (20.4%)	1,209(55.6%)	1,301 (46.5%)
Other	40 (8.9%)	123 (5.7%)	163 (6.2%)
Single	320 (70.8%)	843 (38.7%)	1,163 (44.3%)
Unknown	0 (0.0%)	1 (0.0%)	1 (0.0%)
Duty status*			
Officer	41(9.1%)	300(13.8%)	341(13.0%)
Enlisted	411(90.9%)	1876(86.2%)	2287(87.0%)
Occupation at index			
Communications/Intelligence	161 (35.6%)	449 (20.6%)	610(23.2%)
Engineer	90 (19.9%)	738 (33.9%)	828 (31.5%)
Healthcare	44 (9.7%)	148 (6.8%)	192 (7.3%)
Pilot/Aircrew	14 (3.1%)	142 (6.5%)	156 (5.9%)
Other	143 (31.6%)	699 (32.1%)	842 (32.0%)

* Denotes matching factor

Table 2. Clinical Risk Factors for HIV Infection – Univariate Analysis

	Condition Ever					Condition in the Last 2 Years				
Group	Case (n=452)(%)	Control (n=2176)(%)	Unadjusted Odds Ratio	95% CI	P-value	Case (n=452)(%)	Control (n=2176)(%)	Unadjusted Odds Ratio	95% CI	P-value
STI Diagnosis					0.0018					0.0001
STI History	46 (10.2)	136 (6.3)	1.77	(1.23,2.53)	0.0018	31 (6.9)	68 (3.1)	2.33	(1.50,3.60)	0.0001
No STI History	406 (89.8)	2,040 (93.8)	1.00			421 (93.1)	2,108 (96.9)	1.00		
Ulcerative STI History					0.5654					0.1015
Ulcerative STI History	8 (1.8)	31 (1.4)	1.26	(0.57,2.78)	0.5654	7 (1.5)	16 (0.7)	2.10	(0.86,5.11)	0.1015
No Ulcerative STI History	444 (98.2)	2,145 (98.6)	1.00			445 (98.5)	2,160 (99.3)	1.00		
Non-Ulcerative STI History					0.0022					0.0014
Non-Ulcerative STI History	39 (8.6)	111 (5.1)	1.83	(1.24,2.70)	0.0022	24 (5.3)	55 (2.5)	2.22	(1.36,3.61)	0.0014
No Non-Ulcerative STI History	413 (91.4)	2,065 (94.9)	1.00			428 (94.7)	2,121 (97.5)	1.00		
Substance Abuse Diagnosis					0.1049					0.0600
Substance Abuse History	58 (12.8)	227 (10.4)	1.30	(0.95,1.79)	0.1049	44 (9.7)	158 (7.3)	1.41	(0.99,2.01)	0.0600
No Substance Abuse History	394 (87.2)	1,949 (89.6)	1.00			408 (90.3)	2,018 (92.7)	1.00		
Clinical Signs/Symptoms Diagnosis					<0 .0001					<0.0001
Clinical Signs/Symptoms	316 (69.9)	899 (41.3)	4.75	(3.65,6.19)	<0 .0001	264 (58.4)	531 (24.4)	5.05	(4.00,6.39)	<0.0001
No Clinical Signs/Symptoms	136 (30.1)	1,277 (58.7)	1.00			188 (41.6)	1,645 (75.6)	1.00		
Clinical Syndrome					<0 .0001					<0.0001
Clinical Syndrome	317 (70.1)	1,176 (54.0)	2.59	(1.99,3.38)	<0 .0001	250 (55.3)	683 (31.4)	3.02	(2.42,3.78)	<0.0001
No Clinical Syndrome	135 (29.9)	1,000 (46.0)	1.00			202 (44.7)	1,493 (68.6)	1.00		
MH Diagnosis					<0 .0001					<0.0001
MH History	91 (20.1)	203 (9.3)	2.57	(1.93,3.42)	<0 .0001	58 (12.8)	121 (5.6)	2.61	(1.86,3.67)	<0.0001
No MH History	361 (79.9)	1,973 (90.7)	1.00			394 (87.2)	2,055 (94.4)	1.00		
Medical Encounter History					<0 .0001					<0 .0001
10 or less	128 (28.3)	864 (39.7)	1.00			221 (48.9)	1,441 (66.2)	1.00		
11 – 35	175 (38.7)	837 (38.5)	2.67	(1.88,3.79)	<0 .0001	191 (42.3)	662 (30.4)	2.19	(1,73,2.79)	<0 .0001
> 35	149 (33.0)	475 (21.8)	5.78	(3.76,8.90)	<0 .0001	40 (8.8)	73 (3.4)	4.15	(2.69,6.39)	<0 .0001

CI, confidence interval; STI, Sexually Transmitted Infection; MH, Mental Health

Table 3. Characteristics Retained in Stepwise Multivariate Conditional Logistic Regression Model

Clinical Risk Factor	Odds Ratio	95% Confidence Interval	P-value
Mental Health Diagnosis Ever	1.97	(1.44,2.70)	<0.0001
Clinical Syndrome in the Prior 2 Years	2.23	(1.75,2.84)	<0.0001
Clinical Signs/Symptoms Diagnosis in the Prior 2 Years	4.10	(3.22,5.22)	<0.0001

Figure 1. Proportion of cases and controls with the most common ICD-9 codes for mental health issue, substance abuse, and STI. A) 311: Depressive disorder not elsewhere classified; 309.0: adjustment disorder with depressed mood; 300.00: Anxiety state unspecified; 309.28: adjustment disorder with mixed anxiety and depressed mood. B) 305.1: nondependent tobacco use disorder; 305.00: nondependent alcohol abuse unspecified drinking behavior; 303.90: other and unspecified alcohol dependence unspecified drinking behavior. C) 099.9: venereal disease unspecified; 078.11: *Condyloma acuminatum*; 099.41: other nongonococal urethritis *Chlamydia trachomatis*; 099.40: other nongonococcal urethritis unspecified.